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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/702,676	11/06/2003	Yi Lu	09800080-0078	1656

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EXAMINER	
VIVLEMORE, TRACY ANN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/702,676	LU ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-69,72,74-77,79,80,82 and 95-139* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *95-139* is/are allowed.

6)☒ Claim(s) *63-69,72,74-77,79,80 and 82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Any rejection not reiterated in this Action is withdrawn.

Response to Amendment - Claim Rejections - 35 USC § 112

While the amendment of June 6, 2005 is sufficient to overcome the written description rejection, it is noted that the Examiner's interpretation of the definition of the word "ion" has not been challenged. Thus, for the purposes of examination, the definition of ion "an atom or group of atoms that carries a positive or negative electric charge as a result of having lost or gained one or more electrons" that encompasses not only the metal cations that nucleic acid enzymes known in the art are dependent upon, but also anions including RNA and DNA and inorganic molecules such as chloride, sulfate or phosphate will be applied wherever this word is not more explicitly defined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 74, 76, 79 and 80 are rejected under 35 U.S.C. 102(b) as being anticipated by Breaker et al. (Chemistry & Biology 1994, cited on IDS of 11/03).

1. Claim 74 is drawn to a method of detecting the presence of an ion using a nucleic acid enzyme attached to a support and dependent on Pb^{2+} ions to effect

cleavage of a substrate in the presence of other ions. Claims 76, 79 and 80 limit claim 74 by stating the nucleic acid enzyme is a deoxyribozyme, the substrate contains at least one ribonucleotide and the deoxyribozymes are single strands.

2. Breaker et al. disclose a deoxyribozyme that contains a single ribonucleotide. The deoxyribozyme was selected for its ability to undergo, in the presence of Pb^{2+} ions, self-cleavage at this ribonucleotide, making this portion of the enzyme the substrate (see Results section, first column page 224, last paragraph. Because the selection was carried out in a buffer, the Pb^{2+} ions are in the presence of other ions. The deoxyribozyme contained a biotinylated position that was associated with a streptavidin affinity matrix, a support as defined on page 19 of the instant specification.

3. Thus, Breaker et al. disclose and anticipate claims 74, 76, 79 and 80.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 63-69, 74-77, 79 and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breaker (WO 98/27104, cited on IDS of 11/03) in view of Pan et al. (of record).

4. Claim 63 is drawn to a method of detecting the presence of an ion using a nucleic acid enzyme that is dependent on Pb^{2+} ions to effect cleavage of a substrate in the presence of other ions, wherein the amount of product is measured by fluorescence. Claim 74 is drawn to a similar method where the nucleic acid enzyme is linked to a support and the fluorescence measurement is not required. Claims 64-69, 75, 76, 77, 79 and 80 limit either claim 63 or claim 74 by stating the nucleic acid enzyme is a ribozyme or deoxyribozyme, the enzyme and substrate are separate strands, the substrate contains at least one ribonucleotide and the deoxyribozymes are single strands.

5. Breaker teaches bioreactive allosteric polynucleotides that are catalytic RNA and DNA polynucleotides having catalytic properties with rates that can be controlled by a chemical effector. Such catalytic polynucleotides are created by *in vitro* selection. Breaker teaches at page 1 that the catalytic polynucleotides of the invention are useful as biosensors and that biosensors are widely used for diagnostic purposes. Breaker teaches at page 4, line 6 through page 5, line 7 that such polynucleotides can be attached to a solid support, the chemical effector can be a metal ion and that the

invention provides methods of determining the presence or absence of compounds, illustrated in figure 1 described on page 5. Figure 3A illustrates that the catalytic polynucleotide and the substrate can be separate strands. Breaker teaches at page 14, line 25 through page 15, line 13 that reactions of the catalytic polynucleotides of the invention can be monitored by methods that include fluorescence. An embodiment described on page 16, line 25 through page 17, line 14 teaches that a DNA created to self-cleave in the presence of copper can be used as a sensitive reporter of copper concentration in solution. Breaker does not teach catalytic polynucleotides that function in the presence of Pb^{2+} ions.

6. Pan et al. teach a nucleic acid enzyme created by *in vitro* selection that is a ribozyme that undergoes self-cleavage in the presence of both Mg^{2+} and Pb^{2+} ions (see figure 3). The nucleic acid enzyme disclosed by Pan et al. requires the presence of a metal ion to perform cleavage, so detection of a cleavage product would necessarily indicate the presence of ions in the sample.

7. It would have been obvious to one of ordinary skill in the art at the time of invention to make a catalytic polynucleotide for use as a biosensor as taught by Breaker that functions in the presence of Pb2+ ions as taught by Pan et al. Breaker et al. provide a motivation to do so, teaching that biosensors responsive to chemical effectors such as metal ions have use for diagnostic purposes and also teaching that a catalytic polynucleotide that uses copper as an effector can be used to determine the concentration of copper ions. One of ordinary skill in the art would have had a reasonable expectation of success in producing a catalytic polynucleotide useful as a biosensor that cleaves in the presence of Pb^{2+} ions because Breaker taught that

biosensors responsive to metal ions can be produced using well known and routinely used *in vitro* selection methods and Pan et al. taught an actual catalytic polynucleotide that cleaves in the presence of Pb^{2+} ions.

8. Thus, the invention of claims 63-69, 74-77, 79 and 80 would have been obvious, as a whole, at the time of invention.

Claims 63-69, 72, 74-77, 79, 80 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breaker and Pan et al. as applied to claims 63-69, 74-77, 79 and 80 above, and further in view of Lockhart et al. (US 6,040,138).

9. Claims 63-69, 74-77, 79 and 80 are described in the previous rejection. Claims 72 and 82 depend from claims 63 and 74, respectively, and recite that the nucleic acid enzyme comprises an array of nucleic acid enzymes.

10. The teachings of Breaker and Pan et al. are described above. These references do not teach the use of an array of nucleic acid enzymes.

11. Lockhart et al. teach high density arrays containing oligonucleotide probes suitable for performing large numbers of hybridization assays. Lockhart et al. teach that oligonucleotide probes have long been used to detect complementary nucleic acid sequences in a target nucleic acid of interest and that these probes are sometimes formed as arrays of oligonucleotide probes immobilized on solid supports. Lockhart et al. (see column 6, lines 25-29) define a probe as "an oligonucleotide capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation", a definition that encompasses a nucleic acid enzyme.

12. The teachings of Breaker and Pan et al. are obvious for the reasons described in the previous rejection. It would have been further obvious to one of ordinary skill in the art to provide nucleic acid enzymes as an array attached to a solid support as taught by Lockhart et al. Lockhart et al. provide a motivation to do so, teaching that oligonucleotide probes, which encompass nucleic acid enzymes, have been attached to solid supports for hybridization assays. One of ordinary skill in the art would have had a reasonable expectation of success in providing nucleic acid enzymes as an array on a solid support because Lockhart et al. teach that oligonucleotide probes are routinely used on arrays for hybridization assays and also actually produces arrays having oligonucleotide probes at high density on a support.

13. Thus, the invention of claims 63-69, 72, 74-77, 79, 80 and 82 would have been obvious, as a whole, at the time of invention.

Allowable Subject Matter

Claims 95-139 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811.

On July 15, 2005, the Central FAX Number was changed to 571-273-8300. Faxes sent to the old number (703-872-9306) will be routed to the new number until September 15, 2005.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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Tracy Vivlemore
Examiner
Art Unit 1635

TV
August 15, 2005